I was asked to find a way to further solublize CoQ10 than the 5% that theoretically could be attained in soybean oil, and to use some kind of co-solvent if needed. My first guess was to solublize D-Limonene, because it acts like a total solvent with beeswax – you need ≥ 10% beeswax in formulations that have a high hormone content because it just dissolves the beeswax like it wasn't there. So I took 50g of D-Limonene and started stirring in CoQ10, one or two grams at a time, by hand, and at room temperature. I stopped 40% CoQ10 (20 grams in 50g D-Limonene), although I could have dissolved more in there. After about 30% or so, the solution starts to get a little cloudy after adding the CoQ10, but with 1-3 minutes of steady, slow stirring with a glass rod the CoQ10 completely dissolves and the solution clears up. After getting a clear, dark red 40% solution of CoQ10 in D-Limonene, I wanted to see what would happen when the solution was added to oil, since pure D-Limonene isn't real practical for a softgel fill – although we do make such a product. I added the CoQ w/D-Limonene solution to 50g of soybean oil – 1 or 2g at a time – until I ended up adding the entire amount of CoQ10 solution to the soybean oil. It resulted in a clean, dark red solution, with no precipitation or phase separation at all – we'll see how it is after some time passes; although I don't expect anything bad to occur at all. The final soybean oil/D-Limonene/CoQ10 recovered is 20% of CoQ10 that is completely solublized(sp?).

3/17

The 20% CoQ10 in 50:50 SBO/Limonene shows ~/ -2% precipitated out over the weekend (~ ≤1 gram) _____.

The vial that I added 10% α-lipoic acid shows the same amount of powder at the bottom as on Friday, which is mostly or all α-lipoic acid.

The one containing 10% glycerin still has the glycerin at the bottom, separated, but no other precipitate is evident.

The one containing 10% vitamin, extraordinarily dark (amber, brown) when I first added it which it still is, but no precipitation.

The one I added 10% water to precipitated a very small amount at the interface.

The one containing 10% Lecithin shows no separation or precipitation.

Next I am going to try and make a saturated(?) CoQ10 in Limonene solution and then formulate this to some CoQ10 formulations, without

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3/14/03

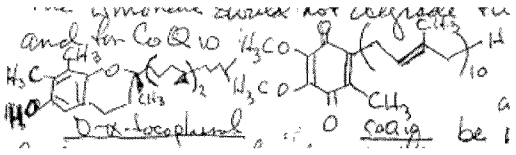
From Page No. 144 any beeswax and see how it comes out and how it behaves after some time passes. The formula for CC-930 (CoSol 100 mg) is:

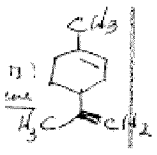
				100 grams:
CO-FA-MX-00016	Coenxyme Q10		104.0900 mg	17.95g.
VI-FA-MX-00191	4-50 Med Tocophenels(sp? 3720/g		269.0300 mg.	46.35 g.
RI-FF-MX-00077	Rice Bran Oil		176.0200 mg.	30.52 a.
BE-PA-MX-00053	Yellow Beeswax		20.0000 mg.	3.45 g
BE-FA-MX-00203	Natural Beta Carotene	255,50000/ g.	10.0500 mg.	1.73 g.
			580,0000 mg.	

I'm going to try, first of all, to remove the Beeswax and the Rice Bran Oil and dissolving the CoQ10 in the same amount of Limonene that would be the weight of the RBO and beeswax, together (196.0200 mg/cip(?)), so there'll be enough to dissolve it, then add the Vitamin E and Beta Carotene. Hopefully, the Vitamin E will help to keep the CoQ10 dissolved like the trial in the small vol I did on Friday. Maybe I'll keep the Beta Carotene out of the formula so I can see it for a few days – then add it. Anyway, here is the formula I will use:

		100 grams:
Coenzyme Q10	104.0900 mg.	17.95 g.
4-20 Med Tocophenels(sp?)	269.0300 mg.	46.35 g.
C-Limonene	196.8300 mg.	33.97 g.
Natural Beta Carotene	10.0500 mg.	1.73 g.
	580.0000 mg.	

The Limonene should not degrade the CoQ10, as the formula for Limonene is:





and for CoQ10: – there is nothing there that will react with each other, so these should be no problem – the Limonene is just acting as an organic solvent – nothing more, nothing less.

Wow! As soon as you add the Vitamin E to it (and it's very light-colored Vitamin E) it turns a dark purple color! I hope it's just due to a change in oxidation state of one or both the Vitamin and CoQ10 – thing isn't anything that should need to change the structure of anything there(?). Made some containing CoQ10//limonene/lecithin (same amt. as the Vit E in the other

one – no discoloring. It looks good. I'm having assays done to see if anything happened. Actually, looking at the _____ _____ involved, I can tell what

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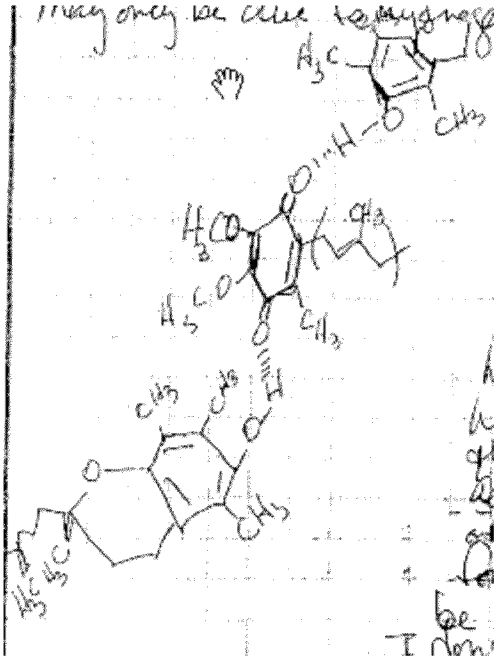
happened: the fully oxidized ketone groups on the quinine moiety(?) of the CoQ10 oxidized the hydroxyl group of the chemenol on the D –α-tocopherol), becoming a semi-quinine – since the CoQ10 is fully solublized and the two molecules are in a compatible solvent, this would happen easily. There is nothing in any of the three molecules that could do anything else (no bond) broken, no acidification or alkalization happening, or anything) – there has just been a change in the oxidation state and the solution absorbs light at a different wavelength, that's all – in fact, it would make both molecules more like their active states, anyways. Actually, its just the way the molecules line up in respect to each other. A similar thing happens to the Shaklee CoQ10 product in the geloil---- it darkens from an orange color to a dark brick red as the CoQ10 becomes more solublized and reacts with the Vitamin E in the product. It doesn't get as dark as this because 1) there isn't as much Vitamin E in the Shaklee product, and 2) the CoQ10 doesn't solublize as much in the Shaklee product – both things happen here, and all the constituents are just as active as they should be.

The mixture that I made last night with lecithin in the place of the Vitamin E looked real good last night, but was very precipitated today – no good. I'm really encouraged with this project, though.

Thinking more on the interaction between the CoQ10 and Vitamin E; it may only be due to hydrogen bonding between the molecules, like this:



Even if the two molecules were, in fact, causing partial oxidation state changes in each other, or if they were hydrogen – bonding either one is fine as far as their function and activity goes, and the only real change in them is not structured, or functional, so I don't see any problem here, other than maybe having to convince some of the less technical ones here about what, in fact, is happening and that the color change is nothing to worry about – actually, if they are just changing the oxidation state of each other, it is only toward the more functional form of both molecules it can only help – I'd be enormously surprised if it were anything else – I don't think anything else is possible.

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Date
3/18/03

From Page No. 146 When I added DL-tocophenyl acetate to the solublized CoQ10/Linomene there was no discoloration – it stayed the clear red color. But after sitting amongst these is a slight amount of precipitation on the bottom of the vial. There is also a slight amount of precipitation on the bottom of the vial & beaker with the D –α-tocopherol and the DL-tocophenyl acetate beaker – 33% CoQ10 appears to be too concentrated – I'll have to bring it down to 30% or 28%, and see how that does.

3/21/03

It's evident that the Limonene is evaporating out of the open beakers, and that may be one of the reasons that I'm getting precipitation – although it is just a small amount (~ 1-2%). Here's an interesting note *in* the beaker that showed some precipitation after a day of sitting out lost more limonene overnight on the second night, but the small amount of precipitation that formed the day before re-solublized spontaneously. The only thing that I can think of that may be causing this is that over the 48 hours or so that the CoQ10 was in the limonene, it needed that much time for a small amount of limonene to completely solublize an even larger amount of CoQ10 – it sounds a bit confusing, but I can't think of any other reason for this happening.

As for the assay I requested on the mix I made that was comparable to our CC-930 100 mg. CoQ Sol, they came out well – the CoQ10 was 110% of claim and the Vitamin E (mixed tocophenols) came out with good results for the separate isomers; in fact the gamma-tocophenol peak was as high as the D-Alpha peak for our dream 4-50 Vitamin E. These were no unexpected peaks in either assay, so it proves my claim that the limonene doesn't hurt any of the substances and that the color change that occurs after adding the vitamin E to the solublized CoQ10 is not due to anything other than a change in oxidation state. I'm very encouraged with all this, and am waiting to hear exactly what they want me to do with it – there's a lot of possibility here, if we do it right.

3/26/03

Now I'm told to go ahead and try solublizing 28-30% CoQ10 in limonene, but they want me to add soybean oil or something to it – just don't like the idea of so much limonene although it won't hurt anything. The mix I made up before – of the 100 mg. CoQSol product – the one that tested out so well, ended up with a small amount of crystals that formed on the bottom of the vial over time, so I'm convinced that the 33% is just too much for it – but adding all that much

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3/19/03

Vitamin E – or anything else increases the chance that the CoQ10 will precipitate out – the one with 33% CoQ10 in limonene and only 10% vitamin E added, back on 3/14 still shows no precipitation, so that's encouraging, but I really don't think we need to add anything else, just the CoQ10 in limonene – the limonene won't hurt anything, and it's already grandfathered in as a safe nutritional supplement ingredient, so there're no regulatory problems with it.

End

Book 3

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